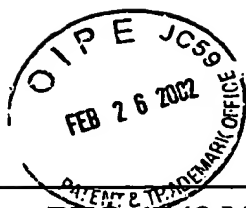


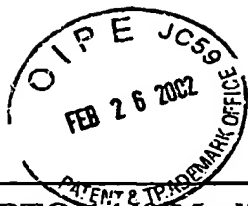


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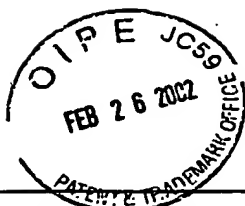
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<i>Gk</i>	AA	Abe, A. et al., "Conformational Energies and the Random-Coil Dimensions and Dipole Moments of Polyoxides $\text{CH}_3\text{O}[(\text{CH}_2)_y\text{O}]_x\text{CH}_3$," <i>J. Am. Chem. Soc.</i> , 1976, 6468-6476	
	AB	Albert, P.R. et al., "Antisense knockouts: molecular scalpels for the dissection of signal transduction", <i>Trends Pharmacol. Sci.</i> , 1994, 15, 250-254	
	AC	Altmann, K. et al., "Second Generation Antisense Oligonucleotides-Inhibition of Pkc-1 And c-RAF Kinase Expression by Chimeric Oligonucleotides Incorporating 6-Substituted Carbocyclic Nucleosides and 2'-O-Ethylene Glycol Substituted Ribonucleosides," <i>Nucleosides & Nucleotides</i> , 1997, 16(7-9), 917-926	
	AD	Altmann, K. et al., "Second-Generation Antisense Oligonucleotides: Structure-Activity Relationships and the Design of Improved Signal-Transduction Inhibitors", <i>Biochem. Soc. Trans.</i> , 1996, 24, 630-637	
	AE	Altmann, K. et al., "Second Generation of Antisense Oligonucleotides: From Nuclease Resistance to Biological Efficacy in Animals," <i>Chimia</i> , 1996, 50, 168-176	
	AF	Baker, B.F. et al., "2'-O-(2-Methoxy)ethyl-modified Anti-intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells", <i>J. Biol. Chem.</i> , 1997, 272, 11994-12000	
	AG	Beal, P. A. et al., "Second Structural Motif for Recognition of DNA by Oligonucleotide-Directed Triple-Helix Formation," <i>Science</i> , 1991, 251, 1360-1363	
	AH	Beaucage, S.L. et al., "Advances in the Synthesis of Oligonucleotides by the Phosphoramidite Approach", <i>Tetrahedron</i> , 1992, 48, 2223-2311	
	AI	Berger et al., "Crystal structures of B-DNA with incorporated 2'-deoxy-2'-fluoro-arabino-furanosyl thymine: implications of conformational preorganization for duplex stability," <i>Nucl. Acids Res.</i> , 1998, 26(10), 2473-2480	
<i>Gk</i>	AJ	Berkow et al. (eds.), <i>The Merck Manual of Diagnosis and Therapy</i> , 15th Edition, Rahway, N.J., 1987, 2263-2277	
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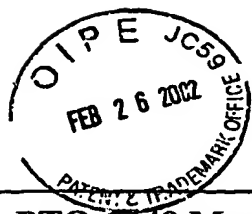
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	AL	Berkow et al. (eds.), <i>The Merck Manual of Diagnosis and Therapy</i> , 15th Edition, Rahway, N.J., 1987, 2286-2293	
	AM	Berkow et al. (eds.), <i>The Merck Manual of Diagnosis and Therapy</i> , 15 th Edition, Rahway, NJ, 1987, 2301-2310	
	AN	Bernhard, E.J. et al., "Direct Evidence Linking Expression of Matrix Metalloproteinase 9 (92-kDa gelatinase/collagenase) to the metastatic phenotype in transformed rat embryo cells," <i>Proc. Natl. Acad. Sci. USA</i> , 1994, 91, 4293-4297	
	AO	Birkedal-Hansen, H. et al., "Proteolytic Remodeling of Extracellular Matrix," <i>Curr. Op. Cell Biol.</i> , 1995, 7, 728-735	
	AP	Bock, L. C. et al., "Selection of Single-Stranded DNA Molecules that Bind and Inhibit Human Thrombin," <i>Nature</i> , 1992, 355, 564-566	
	AQ	Böggemeyer, E. et al., "Borrelia Burgdorferi Upregulates the Adhesion Molecules E-selectin, P-selectin, ICAM-1 and VCAM-1 on Mouse Endothelioma Cells in vitro," <i>Cell Adhes. Commun.</i> , 1994, 2, 145-157	
	AR	Conte, M. R. "Confirmational Properties and Thermodynamics of the RNA Duplex r(CGCAAUUUGCG)2: Comparison with the DNA Analogue d(CGCAAATTTGCG)2," <i>Nucl. Acids Res.</i> , 1997, 25(13), 2627-2634	
	AS	Cornell, W. D. et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules," <i>J. Am. Chem. Soc.</i> , 1995, 117, 5179-5197	
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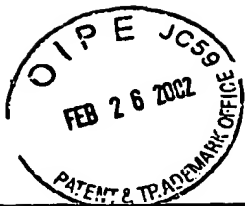
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	AV	Crooke, S.T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", <i>J. Pharmacol. Exp. Therapeutics</i> , 1996, 277, 923-937	
	AW	Crooke, S.T. et al., "Kinetic characteristics of <i>Escherichia coli</i> RNase H1: cleavage of various antisense oligonucleotide-RNA duplexes", <i>Biochem. J.</i> , 1995, 312, 599-608	
	AX	Crooke, S. T. , "Progress in Antisense Therapeutics," <i>Medicinal Research Reviews</i> , 1996, 16(4), 319-344	
	AY	Damha, M.J. et al., "An improved procedure for derivatization of controlled-pore glass beads for solid-phase oligonucleotide synthesis", <i>Nucl. Acids Res.</i> , 1990, 18, 3813-3821	
	AZ	Damha et al., "Hybrids of RNA and Arabinonucleic Acids (ANA and 2'F-ANA) Are Substrates of Ribonuclease H," <i>J. Am. Chem. Soc.</i> , 1998, 120, 12976-12977	
	BA	De Mesmaeker, A. et al., "Antisense Oligonucleotides", <i>Acc. Chem. Res.</i> , 1995, 28, 366-374	
	BB	Dean, N.M. et al., "Inhibition of protein kinase C- α expression in mice after systemic administration of phosphorothioate antisense-oligodeoxynucleotides", <i>Proc. Natl. Acad. Sci.</i> , 1994, 91, 11762-11766	
	BC	DeLisser, H. M. et al., "Molecular and Functional Aspects of PECAM-1/CD31," <i>Immunol. Today</i> , 1994, 15(10), 490-494	
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	BE	Downward, J. et al., "The ras Superfamily of Small GTP-binding proteins," <i>TIBS</i> , 15, 1990, 469-472	
	BF	Egli, M. et al., "RNA Hydration: A Detailed Look," <i>Biochemistry</i> , 1996, 35, 8489-8494	
GLK	BG	Englich, U. et al., "Chemically Modified Oligonucleotides as Probes and Inhibitors", <i>Angew. Chem. Int. Ed. Eng.</i> , 1991, 30, 613-629	
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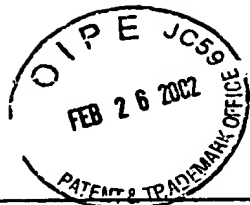
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	BI	Flanagan et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," <i>Nat. Biotechnol.</i> , 1999, 17(1), 48-52	
	BJ	Fraser, A. et al., "Synthesis and Conformational Properties of 2'-Deoxy-2'-methylthio-pyrimidine and -purine Nucleosides: Potential Antisense Applications," <i>J. Heterocycl. Chem.</i> , 1993, 30, 1277-1287	
	BK	Freier, S.M. et al., "The ups and downs of nucleic acid duplex stability: structure-stability studies on chemically-modified DNA:RNA duplexes", <i>Nucl. Acids Res.</i> , 1997, 25, 4429-4443	
	BL	Gaffney, B.L. et al., "A New Strategy for the Protection of Deoxyguanosine During Oligonucleotide Synthesis", <i>Tetrahedron Letts.</i> , 1982, 23, 2257-2260	
	BM	Gao, Y-G. et al., "Molecular Structure of a DNA Decamer Containing an Anticancer Nucleoside Arabinosylcytosine: Conformational Perturbation by Arabinosylcytosine in B-DNA," <i>Biochem.</i> , 1991, 30(41), 9922-9931	
	BN	Gmeiner, W.H. et al., "Effect of Cytarabine on the NMR Structure of a Model Okazaki Fragment from the SV40 Genome," <i>Biochem.</i> , 1999, 38, 1166-1175	
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	BP	Gotfredsen, C.H. et al., "Novel Oligodeoxynucleotide Analogues Containing A 2'-O-Methylarabinonucleoside," <i>Tetra. Lett.</i> , 1994, 35(37), 6941-6944	
	BQ	Gotfredsen, C.H. et al., "Synthesis and Properties of α - and β -Oligodeoxynucleotides Containing α - and β -1-(2-O-Methyl-D-arabino-furanosyl)thymine," <i>Bioorg. Med. Chem.</i> , 1996, 4(8), 1217-1225	
<i>GL</i>	BR	Gotfredsen, C.H. et al., "Structure of a DNA Duplex Containing a Single 2'-O-Methyl- β -D-araT: Combined Use of NMR, Restrained Molecular Dynamics, and Full Relaxation Matrix Refinement," <i>Bioconjugate Chem.</i> , 1996, 7, 680-688	
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	BT	Griffiths, C.E.M. et al., "Keratinocyte Intercellular Adhesion Molecule-1 (ICAM-1) Expression Precedes Derman T Lymphocyte Infiltration in Allergic Contact Dermatitis (<i>Rhus dermatitis</i>)", <i>Am. J. Pathology.</i> , 1989, 135, 1045-1053	
	BU	Gum, R. et al., "Stimulation of 92-kDa Gelatinase B Promoter Activity by ras Is Mitogen-activated Protein Kinase Kinase 1-independent and Requires Multiple Transcription Factor Binding Sites Including Closely Spaced PEA3/ets and AP-1 Sequences," <i>J. Biol. Chem.</i> , 1996, 271(18), 10672-10680	
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	BW	Hakugawa, J. et al., "The Inhibitory Effect of Anti-Adhesion Molecule Antibodies on Eosinophil Infiltration in Cutaneous Late Phase Response in Balb/c Mice Sensitized with Ovalbumin (OVA)," <i>J. Dermatol.</i> , 1997, 24, 73-79	
	BX	Hansske, F. et al., "2' and 3'-Ketonucleosides and their <i>Arabino</i> and <i>Xylo</i> Reduction Products", <i>Tetrahedron</i> , 1984, 40, 125-135	
	BY	Hansske et al., "Nucleic Acid Related Compounds. 43. A Convenient Procedure for the Synthesis of 2' and 3'-Ketonucleosides," <i>Tetra. Lett.</i> , 1983, 24(15), 1589-1592	
	BZ	Hegemann, L. et al., "Biochemical Pharmacology of Protein Kinase C and its Relevance for Dermatology", <i>Pharmacology of the Skin</i> , 1992, Ch. 22, CRC Press, Boca Raton, 357-368	
	CA	Himelstein, B. P. et al., "Metalloproteinases in Tumor Progression: The Contribution of MMP-9," <i>Invasion & Metastasis</i> , 1994-95, 14, 246-258	
	CB	Ho, V.C. et al., "Treatment of severe lichen planus with cyclosporine", <i>J. Am. Acad. Dermatol.</i> , 1990, 22, 64-68	
Gk	CC	Horton, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," <i>J. Mol. Biol.</i> , 1996, 264, 521-533	
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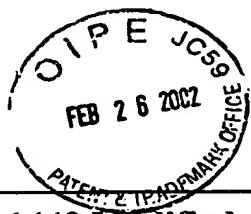
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	CJ	Katocs, A.S. et al., "Biological Testing", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, 1990, Ch. 27, 484-494	
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	CL	Kerr, L. D. et al., "Growth Factors Regulate Transin Gene Expression by c-fos-Dependent and c-fos-Independent Pathways," <i>Science</i> , 1988, 242, 1424-1427	
	CM	Kois, P. et al., "Synthesis and Some Properties of Modified Oligonucleotides. 2. Oligonucleotides Containing 2'-Deoxy-2'-Fluoro-β-D-Arabinofuranosyl Pyrimidine Nucleosides," <i>Nucleosides Nucleotides</i> , 1993, 12(10), 1093-1109	
Gk	CN	Kroschwitz, J.I., "Polynucleotides", <i>Concise Encyclopedia of Polymer Science and Engineering</i> , 1990, John Wiley & Sons, New York, 858-859	
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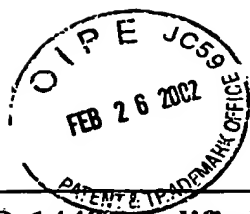
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	CQ	Lesnik, E. A. et al., "Relative Thermodynamic Stability of DNA, RNA, and DNA: RNA Hybrid Duplexes: Relationship with Base Composition and Structure," <i>Biochemistry</i> , 1995 , <i>34(34)</i> , 10807-10815	
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	CU	Lisby, S. et al., "Intercellular adhesion molecule-1 (ICAM-1) expression correlated to inflammation", <i>Br. J. Dermatol.</i> , 1989 , <i>120</i> , 479-484	
	CV	Litwin, M. et al., "Novel Cytokine-independent Induction of Endothelial Adhesion Molecules Regulated by Platelet/Endothelial Cell Adhesion Molecule (CD31)," <i>J. Cell Biol.</i> , 1997 , <i>139(1)</i> , 219-228	
	CW	Manoharan, M. et al., "Lipidic Nucleic Acids", <i>Tetrahedron Letts.</i> , 1995 , <i>36</i> , 3651-3654	
	CX	Manoharan M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications", <i>Bioorganic Med. Chem. Letts.</i> , 1994 , <i>4</i> , 1053-1060	
Gk	CY	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", <i>Nucleosides and Nucleotides</i> , 1995 , <i>14</i> , 969-973	
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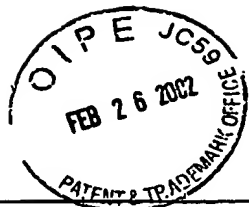
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	DC	Matsuda, A. et al., "Nucleosides and Nucleotides. 97. Synthesis of New Broad Spectrum Antineoplastic Nucleosides, 2'-Deoxy-2'-methylidenecytidine (DMDC) and Its Derivatives," <i>J. Med. Chem.</i> , 1991, 34, 812-819	
	DD	Miller, P.S. et al., "A New approach to chemotherapy based on molecular biology and nucleic acid chemistry: Matagen (masking tape for gene expression)", <i>Anti-Cancer Drug Des.</i> , 1987, 2, 117-128	
	DE	Milligan, J. F. et al., "Current Concepts in Antisense Drug Design," <i>J. Med. Chem.</i> , 1993, 36(14), 1923-1937	
	DF	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorothioate antisense oligonucleotides by LDL-mediated delivery", <i>Biochim. et Biophysica</i> , 1995, 1264, 229-237	
	DG	Monia, B.P. et al., "Sequence-specific Antitumor Activity of a Phosphorothioate Oligodeoxyribonucleotide Targeted to Human C-raf Kinase Supports an Antisense Mechanism of Action In Vivo," <i>Proc. Natl. Acad. Sci. USA</i> , 1996, 93, 15481-15483	
	DH	Newman, P. J. et al., "Perspective Series: Cell Adhesion in Vascular Biology," <i>Biology PECAM-1, J. Clin. Invest.</i> , 1997, 99(1), 3-7	
6k	DI	Nies, A.S. et al., "Principles of Therapeutics", <i>Goodman & Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, 1996, Ch. 3, 43-62	
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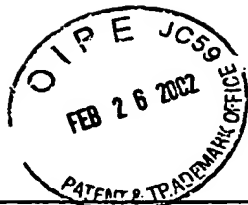


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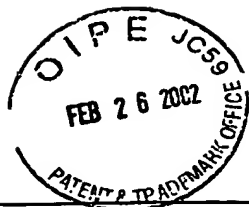
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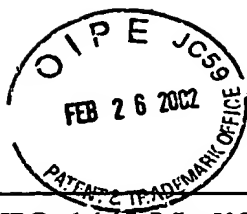
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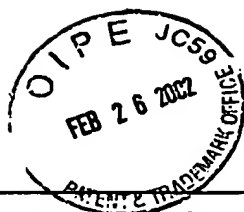


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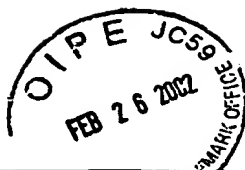


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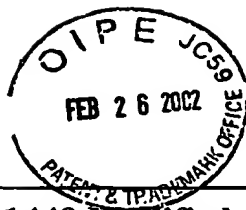
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Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office	Docket No. ISIS-4789	Serial No. 09/970,971
	Applicant Manoharan et al.	
	Filing Date October 4, 2001	Group Not yet assigned

U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
GK	HN	5,580,767	12/03/96	Cowsert et al.	435	172.3
	HO	5,582,972	12/10/96	Lima et al.	435	6
	HP	4,381,344	04/1983	Rideout et al.	435	87
	HQ	5,013,830	05/07/91	Ohtsuka et al.	536	27
	HR	5,134,066	07/28/92	Rogers et al.	435	91
	HS	5,212,295	05/18/93	Cook	536	26.7
	HT	5,214,135	05/25/93	Srivastava et al.	536	26.7
	HU	5,466,786	11/14/95	Buhr et al.	536	26.26
	HV	5,658,731	08/19/97	Sproat et al.	435	6
	HW	5,672,695	09/30/97	Eckstein et al.	536	24.5
GK	HX	5,698,687	12/16/97	Eckstein et al.	536	25.3

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES NO	
GK	HY	2,017,369	05/23/90	Canada	X	
GK	HZ	0 260 032	08/27/87	EP	X	
GK	IA	0 287 313	10/19/88	EP	X	
	IB	0-399-330	05/15/90	EP		X
GK	IC	0 417 999	03/10/91	EP	X	

EXAMINER <i>G. K. Gish</i>	DATE CONSIDERED <i>5/10/06</i>
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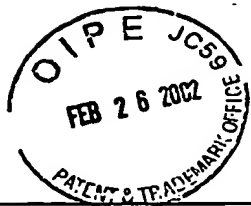
U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
GK	ID	5,245,022	09/14/93	Weis et al.	536	24
	IE	5,627,053	05/06/97	Usman et al.	435	91
	IF	5,639,647	06/17/97	Usman et al.	435	199
	IG	5,817,635	10/06/98	Eckstein et al.	514	44
GK	IH	5,859,221	01/12/99	Cook et al.	536	23

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation YES NO	
GK	II	39 15462 A1	06/09/90	Germany	considered Derwent English Abstract	X
	IJ	41 10085 A1	10/01/92	Germany	considered Derwent English Abstract	X
	IK	WO 90/15814	12/27/90	PCT		
	IL	WO 91/06556	05/16/91	PCT		
	IM	WO 91/15499	10/17/91	PCT	considered Derwent English Abstract	X
	IN	WO 92/07065	04/30/92	PCT		
	IO	339 842	11/02/89	EP		
	IP	0 552 178 B1	01/02/97	EP		
GK	IQ	1 205 021	05/27/86	Canada		

EXAMINER <i>G. Krishnan</i>	DATE CONSIDERED <i>5/10/06</i>
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				Applicant Manoharan et al.			
				Filing Date October 4, 2001		Group Not yet assigned	
U. S. PATENT DOCUMENTS							
Examiner Initial		Document No.	Date	Name	Class	Subclass	
HC	IR	5,582,986	12/10/96	Monia et al.	435	6	
	IS	5,591,600	01/07/97	Ecker	435	69.1	
	IT	5,591,623	01/07/97	Bennett et al.	435	240.2	
	IU	5,591,720	01/07/97	Anderson et al.	514	44	
	IV	5,607,923	03/04/97	Cook et al.	514	44	
	IW	5,620,963	04/15/97	Cook et al.	514	44	
	IX	5,639,649	06/17/97	Almond et al.	435	235.1	
	IY	5,658,891	08/19/97	Draper et al.	514	44	
	IZ	5,661,134	08/26/97	Cook et al.	514	44	
	JA	5,681,747	10/28/97	Boggs et al.	435	375	
	JB	5,681,944	10/28/97	Crooke et al.	536	24.5	
	JC	5,877,309	03/02/99	McKay et al.	536	24.5	
	JD	5,985,558	11/16/99	Dean et al.	435	6	
	JE	5,955,443	09/21/99	Bennett et al.	514	44	
	JF	6,111,094	08/29/00	Bennett et al.	536	24.5	
	JG	5,334,711	08/02/94	Sproat, et al.	536	24.5	
	JH	6,300,491	10/09/01	Bennett et al.	536	24.5	
	JI	5,670,633	09/23/97	Cook et al.	536	23.1	
JK	JJ	6,307,040	10/23/01	Cook et al.	536	24.5	
EXAMINER <i>G. Krishnan</i>				DATE CONSIDERED <i>5/10/06</i>			